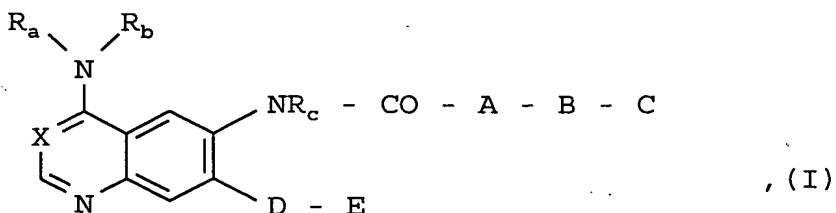


Patent Claims

1. Bicyclic heterocycles of general formula



wherein

$R_a$  denotes a hydrogen atom or a methyl group,

$R_b$  denotes a phenyl, benzyl- or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups  $R_1$  to  $R_3$ , while

$R_1$  and  $R_2$ , which may be identical or different, in each case denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

a methyl, ethyl, hydroxy, methoxy, ethoxy, amino, cyano, vinyl or ethynyl group,

an aryl, aryloxy, arylmethyl or arylmethoxy group,

a methyl or methoxy group substituted by 1 to 3 fluorine atoms or

$R_1$  together with  $R_2$ , if they are bound to adjacent carbon atoms, denote a  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{NH}-$  or  $-\text{CH}=\text{N}-\text{NH}$  group and

$R_3$  denotes a hydrogen, fluorine, chlorine or bromine atom,

$R_c$  denotes a hydrogen atom or a methyl group,

X denotes a methyne group substituted by a cyano group or a nitrogen atom,

A denotes a 1,1- or 1,2-vinylene group which may be substituted in each case by one or two methyl groups or by a trifluoromethyl group,

an ethynylene group or

a 1,3-butadien-1,4-ylene group optionally substituted by a methyl or trifluoromethyl group,

B denotes an alkylene or -CO-alkylene group wherein the alkylene moiety in each case contains 1 to 4 carbon atoms, while the linking of the -CO-alkylene group to the adjacent group A in each case must take place via the carbonyl group,

a -CO-O-alkylene- or -CO-NR<sub>4</sub>-alkylene group wherein the alkylene moiety in each case contains 1 to 4 carbon atoms, while the linking to the adjacent group A in each case must take place via the carbonyl group, wherein

R<sub>4</sub> denotes a hydrogen atom or a methyl or ethyl group,

or a carbonyl group,

C denotes a 2-oxo-morpholin-4-yl group substituted by the group R<sub>5</sub> or by the group R<sub>5</sub> and a C<sub>1-4</sub>-alkyl group, while

R<sub>5</sub> denotes a C<sub>3-4</sub>-alkyl, hydroxy-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkoxy-C<sub>1-4</sub>-alkyl, di-(C<sub>1-4</sub>-alkyl)-amino-C<sub>1-4</sub>-alkyl, pyrrolidino-C<sub>1-4</sub>-alkyl, piperidino-C<sub>1-4</sub>-alkyl, morpholino-C<sub>1-4</sub>-alkyl, 4-(C<sub>1-4</sub>-alkyl)-piperazino-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkylsulphanyl-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkylsulphonyl-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkylsulphonyl-C<sub>1-4</sub>-alkyl, cyano-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkoxycarbonyl-C<sub>1-4</sub>-alkyl, aminocarbonyl-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyl-aminocarbonyl-C<sub>1-4</sub>-alkyl,

di-(C<sub>1-4</sub>-alkyl)aminocarbonyl-C<sub>1-4</sub>-alkyl, pyrrolidinocarbonyl-C<sub>1-4</sub>-alkyl, piperidinocarbonyl-C<sub>1-4</sub>-alkyl, morpholinocarbonyl-C<sub>1-4</sub>-alkyl or a 4-(C<sub>1-4</sub>-alkyl)-piperazinocarbonyl-C<sub>1-4</sub>-alkyl group,

a 2-oxo-morpholin-4-yl group substituted by two groups R<sub>5</sub>, where R<sub>5</sub> is as hereinbefore defined and the two groups R<sub>5</sub> may be identical or different,

a 2-oxo-morpholin-4-yl group, wherein the two hydrogen atoms of a methylene group are replaced by a -(CH<sub>2</sub>)<sub>m</sub>, -CH<sub>2</sub>-Y-CH<sub>2</sub>, -CH<sub>2</sub>-Y-CH<sub>2</sub>-CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>-Y-CH<sub>2</sub>CH<sub>2</sub>- or -CH<sub>2</sub>CH<sub>2</sub>-Y-CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>- bridge optionally substituted by one or two C<sub>1-2</sub>-alkyl groups, while

m denotes the number 2, 3, 4, 5 or 6 and

Y denotes an oxygen or sulphur atom, a sulphinyl, sulphonyl or C<sub>1-4</sub>-alkylimino group,

a 2-oxo-morpholin-4-yl group, wherein a hydrogen atom in the 5 position together with a hydrogen atom in the 6 position is replaced by a -(CH<sub>2</sub>)<sub>n</sub>, -CH<sub>2</sub>-Y-CH<sub>2</sub>, -CH<sub>2</sub>-Y-CH<sub>2</sub>CH<sub>2</sub>- or -CH<sub>2</sub>CH<sub>2</sub>-Y-CH<sub>2</sub>- bridge, while

Y is as hereinbefore defined and

n denotes the number 2, 3 or 4,

or, if D together with E denotes a group R<sub>d</sub>, it may also denote a 2-oxo-morpholin-4-yl group which may be substituted by 1 to 4 C<sub>1-2</sub>-alkyl groups,

D denotes a -O-C<sub>1-6</sub>-alkylene group, while the alkylene moiety is linked to the group E, or

an oxygen atom, while this may not be linked to a nitrogen atom of the group E, and

E denotes an amino group substituted by 2 C<sub>1-4</sub>-alkyl groups, wherein the alkyl groups may be identical or different and each alkyl moiety may be substituted from the 2 position by a C<sub>1-4</sub>-alkoxy or di-(C<sub>1-4</sub>-alkyl)-amino group or by a 4- to 7-membered alkyleneimino group, while in the abovementioned 6- to 7-membered alkyleneimino groups in each case a methylene group may be replaced in the 4 position by an oxygen or sulphur atom or by a sulphinyl, sulphonyl- or N-(C<sub>1-4</sub>-alkyl)-imino group,

a 4- to 7-membered alkyleneimino group optionally substituted by 1 to 4 methyl groups,

a 6- to 7-membered alkyleneimino group optionally substituted by 1 or 2 methyl groups, wherein in each case a methylene group in the 4 position is replaced by an oxygen or sulphur atom or by a sulphinyl, sulphonyl- or N-(C<sub>1-4</sub>-alkyl)-imino group,

an imidazolyl group optionally substituted by 1 to 3 methyl groups,

a C<sub>5-7</sub>-cycloalkyl group, wherein a methylene group is replaced by an oxygen or sulphur atom or by a sulphinyl, sulphonyl or N-(C<sub>1-4</sub>-alkyl)-imino group, or

D together with E denotes a hydrogen atom,

a C<sub>1-6</sub>-alkoxy group optionally substituted from the 2 position by a hydroxy- or C<sub>1-4</sub>-alkoxy group,

a C<sub>3-7</sub>-cycloalkoxy- or C<sub>3-7</sub>-cycloalkyl-C<sub>1-4</sub>-alkoxy group,

or a group R<sub>d</sub>, where

$R_d$  denotes a  $C_{2-6}$ -alkoxy group which is substituted from the 2 position by a  $C_{4-7}$ -cycloalkoxy- or  $C_{3-7}$ -cycloalkyl- $C_{1-3}$ -alkoxy group,

a  $C_{4-7}$ -cycloalkoxy- or  $C_{3-7}$ -cycloalkyl- $C_{1-6}$ -alkoxy group wherein the cycloalkyl moiety in each case is substituted by a  $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkoxy, di- $(C_{1-4}$ -alkyl)-amino, pyrrolidino, piperidino, morpholino, piperazino, 4- $(C_{1-2}$ -alkyl)-piperazino,  $C_{1-4}$ -alkoxy- $C_{1-2}$ -alkyl, di- $(C_{1-4}$ -alkyl)-amino- $C_{1-2}$ -alkyl, pyrrolidino- $C_{1-2}$ -alkyl, piperidino- $C_{1-2}$ -alkyl, morpholino- $C_{1-2}$ -alkyl, piperazino- $C_{1-2}$ -alkyl- or 4- $(C_{1-2}$ -alkyl)-piperazino- $C_{1-2}$ -alkyl group, while the abovementioned cycloalkyl moieties may additionally be substituted by a methyl or ethyl group,

while, unless otherwise stated, by the aryl moieties mentioned in the definition of the abovementioned groups is meant a phenyl group which may be mono- or disubstituted by  $R_6$ , while the substituents may be identical or different and

$R_6$  denotes a fluorine, chlorine, bromine or iodine atom, a  $C_{1-2}$ -alkyl, trifluoromethyl or  $C_{1-2}$ -alkoxy group, or

two groups  $R_6$ , if they are bound to adjacent carbon atoms, together represent a  $C_{3-4}$ -alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

the tautomers, stereoisomers and salts thereof.

2. Bicyclic heterocycles of general formula I according to claim 1, wherein

$R_a$  denotes a hydrogen atom,

$R_b$  denotes a benzyl or 1-phenylethyl group or a phenyl group substituted by the groups  $R_1$  and  $R_2$ , while

$R_1$  denotes a hydrogen, fluorine, chlorine or bromine atom, a methyl, trifluoromethyl, cyano or ethynyl group and  $R_2$  denotes a hydrogen or fluorine atom,

$R_c$  denotes a hydrogen atom,

X denotes a nitrogen atom,

A denotes a 1,2-vinylene group,

B denotes a  $C_{1-4}$ -alkylene group,

C denotes a 2-oxo-morpholin-4-yl group substituted by the group  $R_5$  or by the group  $R_5$  and a  $C_{1-4}$ -alkyl group, while

$R_5$  denotes a  $C_{3-4}$ -alkyl,  $C_{1-2}$ -alkoxy- $C_{1-4}$ -alkyl, di- $(C_{1-2}$ -alkyl)-amino- $C_{1-4}$ -alkyl, pyrrolidino- $C_{1-4}$ -alkyl, piperidino- $C_{1-4}$ -alkyl, morpholino- $C_{1-4}$ -alkyl, 4- $(C_{1-2}$ -alkyl)-piperazino- $C_{1-4}$ -alkyl,  $C_{1-2}$ -alkylsulphanyl- $C_{1-4}$ -alkyl,  $C_{1-2}$ -alkylsulphinyl- $C_{1-4}$ -alkyl,  $C_{1-2}$ -alkylsulphonyl- $C_{1-4}$ -alkyl, cyano- $C_{1-4}$ -alkyl,  $C_{1-2}$ -alkoxycarbonyl- $C_{1-4}$ -alkyl, aminocarbonyl- $C_{1-4}$ -alkyl,  $C_{1-2}$ -alkyl-aminocarbonyl- $C_{1-4}$ -alkyl, di- $(C_{1-2}$ -alkyl)-aminocarbonyl- $C_{1-4}$ -alkyl, pyrrolidinocarbonyl- $C_{1-4}$ -alkyl, piperidinocarbonyl- $C_{1-4}$ -alkyl, morpholinocarbonyl- $C_{1-4}$ -alkyl or a 4- $(C_{1-2}$ -alkyl)-piperazinocarbonyl- $C_{1-4}$ -alkyl group,

a 2-oxo-morpholin-4-yl group substituted by two groups  $R_5$ , while  $R_5$  is as hereinbefore defined and the two groups  $R_5$  may be identical or different,

a 2-oxo-morpholin-4-yl group, wherein the two hydrogen atoms of a methylene group are replaced by a  $-(CH_2)_m$ ,  $-CH_2-Y-CH_2$ ,  $-CH_2-Y-CH_2-CH_2-$  or  $-CH_2CH_2-Y-CH_2CH_2-$  bridge, while

m denotes the number 2, 3, 4 or 5 and

Y denotes an oxygen or sulphur atom, a sulphinyl, sulphonyl or  $C_{1-2}$ -alkylimino group,

a 2-oxo-morpholin-4-yl group, wherein a hydrogen atom in the 5 position together with a hydrogen atom in the 6 position is replaced by a  $-(CH_2)_n$ ,  $-CH_2-Y-CH_2$ ,  $-CH_2-Y-CH_2CH_2-$  or  $-CH_2CH_2-Y-CH_2-$  bridge, where

Y is as hereinbefore defined and  
n denotes the number 2, 3 or 4,

or, if D together with E denotes a group  $R_d$ , it may also denote a 2-oxo-morpholin-4-yl group which may be substituted by 1 or 2 methyl or ethyl groups,

D denotes a  $-O-C_{1-4}$ -alkylene group, while the alkylene moiety is linked to the group E, and

E denotes a dimethylamino, diethylamino, pyrrolidino, piperidino, morpholino, 4-methyl-piperazino- or 4-ethyl-piperazino group or

D together with E denotes a hydrogen atom,

a methoxy, ethoxy, 2-methoxy-ethoxy, 3-methoxy-propyloxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy or tetrahydropyranylmethoxy group,

a cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cyclopropylmethoxy, cyclobutylmethoxy, cyclopentylmethoxy or cyclohexylmethoxy group or

a group  $R_d$ , where

$R_d$  denotes a 2-(cyclobutyloxy)-ethoxy, 2-(cyclopentyloxy)-ethoxy, 2-(cyclopropylmethoxy)-ethoxy or 2-(cyclobutylmethoxy)-ethoxy group,

the tautomers, stereoisomers and salts thereof.

3. Bicyclic heterocycles of general formula I according to claim 1, wherein

R<sub>a</sub> denotes a hydrogen atom,

R<sub>b</sub> denotes a 1-phenylethyl, 3-methylphenyl, 3-chlorophenyl, 3-bromophenyl- or 3-chloro-4-fluorophenyl group,

R<sub>c</sub> denotes a hydrogen atom,

X denotes a nitrogen atom,

A denotes a 1,2-vinylene group,

B denotes a methylene group,

C denotes a 2-oxo-morpholin-4-yl group which is substituted by a methoxymethyl, methoxyethyl, ethoxymethyl, ethoxyethyl, dimethylaminomethyl, dimethylaminoethyl, diethylaminomethyl, diethylaminoethyl, cyanomethyl or cyanoethyl group,

a 2-oxo-morpholin-4-yl group, wherein the two hydrogen atoms of a methylene group are replaced by a -CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>-O-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>-NCH<sub>3</sub>-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>-NC<sub>2</sub>H<sub>5</sub>-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>-O-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>-NCH<sub>3</sub>-CH<sub>2</sub>CH<sub>2</sub>- or -CH<sub>2</sub>CH<sub>2</sub>-NC<sub>2</sub>H<sub>5</sub>-CH<sub>2</sub>CH<sub>2</sub>- bridge,

a 2-oxo-morpholin-4-yl group, wherein a hydrogen atom in the 5 position together with a hydrogen atom in the 6 position is replaced by a -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>-O-CH<sub>2</sub>, -CH<sub>2</sub>-NCH<sub>3</sub>-CH<sub>2</sub>, -CH<sub>2</sub>-NC<sub>2</sub>H<sub>5</sub>-CH<sub>2</sub>, -CH<sub>2</sub>-O-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>-NCH<sub>3</sub>-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>-NC<sub>2</sub>H<sub>5</sub>-CH<sub>2</sub>CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>-O-CH<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>-NCH<sub>3</sub>-CH<sub>2</sub>- or -CH<sub>2</sub>CH<sub>2</sub>-NC<sub>2</sub>H<sub>5</sub>-CH<sub>2</sub>- bridge,



or, if D together with E denotes a group  $R_d$ , it may also denote a 2-oxo-morpholin-4-yl group which is substituted by 1 or 2 methyl groups, and

D together with E denotes a hydrogen atom,

a methoxy, ethoxy, 2-methoxy-ethoxy, 3-methoxy-propyloxy, tetrahydrofuran-3-yloxy, tetrahydropyran-4-yloxy or tetrahydrofuranylmethoxy group,

a cyclobutyloxy, cyclopentyloxy, cyclopropylmethoxy, cyclobutylmethoxy or cyclopentylmethoxy group or

a group  $R_d$ , where

$R_d$  denotes a 2-(cyclobutyloxy)-ethoxy, 2-(cyclopentyloxy)-ethoxy, 2-(cyclopropylmethoxy)-ethoxy or 2-(cyclobutylmethoxy)-ethoxy group,

the tautomers, stereoisomers and salts thereof.

4. Bicyclic heterocycles of general formula I according to claim 1, wherein

$R_a$  denotes a hydrogen atom,

$R_b$  denotes a 3-chloro-4-fluorophenyl group,

$R_c$  denotes a hydrogen atom,

X denotes a nitrogen atom,

A denotes a 1,2-vinylene group,

B denotes a methylene group,

C denotes a 2-oxo-morpholin-4-yl group which is substituted by a methoxymethyl or methoxyethyl group, or

a 2-oxo-morpholin-4-yl group, wherein the two hydrogen atoms of a methylene group are replaced by a  $-\text{CH}_2\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-$  bridge, and

D together with E denotes a hydrogen atom, a methoxy or cyclopropylmethoxy group,

the tautomers, stereoisomers and salts thereof.

5. The following compounds of general formula I according to claim 1:

(1) 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{[4-((R)-2-methoxymethyl-6-oxo-morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-cyclopropylmethoxy-quinazoline,

(2) 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{[4-(2-oxo-1,9-dioxo-4-aza-spiro[5.5]undec-4-yl)-1-oxo-2-buten-1-yl]amino}-7-cyclopropylmethoxy-quinazoline and

(3) 4-[(3-chloro-4-fluoro-phenyl)amino]-6-({4-[2-(2-methoxyethyl)-6-oxo-morpholin-4-yl]-1-oxo-2-buten-1-yl}amino)-7-cyclopropylmethoxy-quinazoline,

the tautomers, stereoisomers and salts thereof.

6. Physiologically acceptable salts of the compounds according to at least one of claims 1 to 5 with inorganic or organic acids or bases.

7. Pharmaceutical compositions containing a compound according to at least one of claims 1 to 5 or a physiologically acceptable salt according to claim 6 optionally together with one or more inert carriers and/or diluents.

10. Process for preparing the compounds of general formula I according to claims 1 to 6, characterised in that

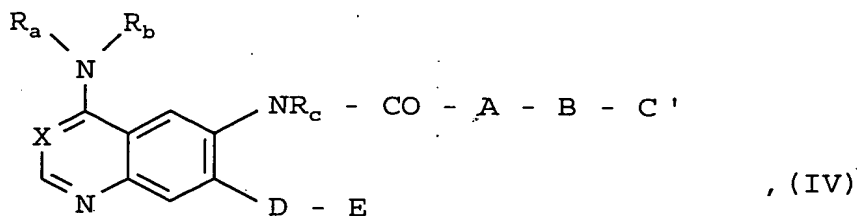
$$\begin{array}{c}
 R_a \quad R_b \\
 \diagdown \quad / \\
 N \\
 | \\
 X \text{---} C \text{---} C \text{---} C \text{---} C \text{---} C \text{---} C \\
 | \quad \quad \quad | \quad \quad \quad | \quad \quad \quad | \\
 N \quad \quad \quad D - E \quad \quad \quad NR_c - CO - A - B - Z_1
 \end{array}
 \quad , \text{ (II)}$$

$R_a$  to  $R_c$ ,  $A$ ,  $B$ ,  $D$ ,  $E$  and  $X$  are defined as in claims 1 to 5 and  $Z_1$  denotes a leaving group,

$$\text{H} - \text{C} \quad , \text{ (III)}$$

C is defined as in claims 1 to 5 hereinbefore, or

b) a compound of general formula



optionally formed in a reaction mixture

wherein

$R_a$  to  $R_c$ , A, B, D, E and X are defined as in claims 1 to 5 and C' denotes a correspondingly substituted N-(carboxymethyl)-N-(2-hydroxyethyl)-amino or N-( $C_{1-4}$ -alkyloxycarbonylmethyl)-N-(2-hydroxyethyl)-amino group which can be converted into a group C by cyclising, is cyclised, and

if necessary any protecting group used in the reactions described above is cleaved again and/or

if desired a compound of general formula I thus obtained is resolved into its stereoisomers and/or

a compound of general formula I thus obtained is converted into the salts thereof, particularly, for pharmaceutical use, into the physiologically acceptable salts thereof.